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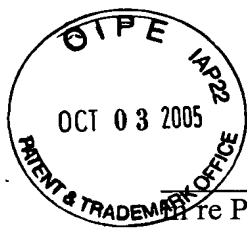
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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) HO-P02149US0	
	Application Number 09/830,795-Conf. #3545	Filed October 29, 1999	
	First Named Inventor Martin Stjernstrom		
	Art Unit 1743	Examiner D. K. Handy	
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <p><input type="checkbox"/> applicant /inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input type="checkbox"/> attorney or agent of record. Registration number _____</p> <p><input checked="" type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. <u>45,872</u></p> <p> _____ Signature</p> <p><u>Melissa W. Acosta, Ph.D.</u> _____ Typed or printed name</p> <p><u>(713) 651-5407</u> _____ Telephone number</p> <p><u>October 3, 2005</u> _____ Date</p> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			

<input type="checkbox"/> *Total of <u>1</u> forms are submitted.
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Docket No.: HO-P02149US0  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Re Patent Application of:

Martin Stjernstrom

Application No.: 09/830,795

Art Unit: 1743

Filed: October 29, 1999

Examiner: Handy, Dwayne K.

For: LIQUID MICROVOLUME HANDLING  
SYSTEM

MS AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**Pre-Appeal Brief Request for Review**

The outstanding issues in this application are as follows:

- Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989).
- Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469).

**I. 35 U.S.C. 103(a) rejection over Litborn in view of Williams et al.**

Claims 6-8, 10, 12, and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) in view of Williams et al. (5,171,989).

*NON-ANALOGOUS ART*

To combine two or more references for a 103(a) rejection, the references must be analogous art. *See* MPEP 2141.01(a). While Litborn is relevant to the art of preventing evaporation from small liquid samples, Williams deals with sample feeding into a laser desorption time of flight mass spectrometer. Williams is thus not technologically nor topically analogous art. Art may also be considered analogous if it is relevant to the particular problem addressed in the application under examination. *See* MPEP 2141.01(a); *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1069, 68 USPQ2d 1481, 1490 (Fed. Cir. 2003). In the Examiner's Final Office Action 05-03-2005 (Paper Number not provided), the Examiner attempts to establish Williams as analogous art.

The Examiner makes the assertion that Williams' method of adding of ethylene glycol to aqueous samples to improve sample freezing would somehow commend itself to one of skill trying to implement a variation of Litborn where the immiscible cover layer exchanges compounds with the sample fluid. (Examiner's Final Office Action 05-03-2005, paragraph 6). The Examiner does not explain how adding ethylene glycol or any other sample miscible liquid would improve "mixing" with the immiscible cover fluid in Litborn. More fundamentally, the Examiner states that the teachings of Williams are "reasonably pertinent to the problem of trying to move compounds between two phases that are already in contact...." Assuming *arguendo* that this is true, it is completely irrelevant. Improving mixing or the exchange of compounds between phases is not a problem addressed or at issue in the microfluidic device of this application. The Examiner provides no explanation as to why one of skill in the art would look to Williams to solve the problem of fluid evaporation and sample volume stability in a microfluidic device. The Examiner's obscure statement that "[t]his led Examiner to Williams" does not amount to a reasoned basis for asserting Williams as analogous art. (Examiner's Final Office Action 05-03-2005, paragraph 5). Absent a cogent basis for establishing Williams as analogous art, it is improper to combine Litborn and Williams. Thus the Examiner has not met his burden for a *prima facie* case of obviousness.

#### *COMBINATIONS CANNOT ALTER PRINCIPLE OF OPERATION OR RENDER COMBINATION INOPERATIVE*

The Examiner has indicated that Litborn does not teach the use of a cover liquid that is miscible with the sample liquid. (Examiner's Office Action 09-29-2004, paragraph 2). The Examiner has also indicated that Williams does not address evaporation prevention and indicated that this was not necessary since Litborn addresses evaporation. (Examiner's Final Office Action 05-03-2005, paragraph 5). The evaporation prevention taught in Litborn is completely distinct and unrelated to the claims of the present invention where evaporation is allowed, but the liquid volume disappearing by evaporation is replenished. Instead, Litborn requires an additional liquid, a covering liquid, that is immiscible with the sample liquid. To combine the continuous fluid addition element of Williams with the immiscible cover layer of Litborn would render the combination inoperative. Because the cover layer of Litborn prevents evaporation, the addition of a continuous feed of another liquid miscible, e.g., ethylene glycol, with the sample liquid would result in a gradually increased sample volume. This is incompatible with the need for sample volume stability in Litborn. Alternatively, were the continuously fed miscible fluid of Williams substituted for the immiscible cover layer of Litborn, this would impermissibly alter the principle of operation in Litborn for preventing evaporational loss of sample volume. Yet further, the Examiner also does not address the fact that the covering of liquid of Litborn is preferably a liquid that has a low boiling point, for example the boiling point for the covering liquid is preferably at most 10°C above the operation temperature (See page 9, line 11). Thus, the covering liquids of Litborn have a low boiling point, which is the exact opposite of the preferred liquid or solvent of Williams, which is ethylene glycol having a boiling point of 197.3°C. Assuming the operation temperature of Litborn is performed at 95°C, the covering liquid would only have a boiling point of 105°C, which is well below the boiling point of ethylene glycol. Thus, the compounds of Litborn and Williams are not analogous and would not be expected to perform similar functions nor would one of skill in the art believe that they could be substituted for one another. Because these two references may not be combined, the Examiner has not met his burden for a *prima facie* case of obviousness.

## NO MOTIVATION TO COMBINE

When an obviousness determination is based on multiple prior art references, there must be a showing of some teaching, suggestion or reason to combine the references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." MPEP 2143.01. In response to Applicant's request for the Examiner to specifically identify a suggestion to combine the references, the Examiner referred in Litborn to claim 9; page 9, lines 23-26 and 31-34; claims 10 and 11; and page 9, lines 27-30. The Examiner then asserted that these portions of Litborn "suggest a mixing of the solvent and sample phases would be desirable..." (Examiner's Final Office Action 05-03-2005, paragraph 5).

The Examiner's citation fails to substantiate his *prima facie* case of obviousness on two levels. Factually, the Examiner is simply in error. There is no "solvent phase" added to the sample in Litborn but rather an immiscible cover layer on top of the sample (e.g. mineral oil over a PCR reaction). Claims 9-11 of Litborn all depend on claim 1 which is specifically limited to immiscible liquids. The Examiner's attempt to broaden the scope of these claims to encompass mixing of the erroneously dubbed "solvent" phase with the sample phase is untenable. Based on this erroneous interpretation of Litborn, the Examiner was somehow "led" to Williams. In Williams, the Examiner learns that one can add miscible fluids having high boiling points, such as ethylene glycol, to an aqueous sample and change the combined fluid's properties relative to the original sample. (Examiner's Final Office Action 05-03-2005, paragraph 5). The Examiner then determines that this teaching in Williams would be useful in enabling the "mixing" of the nonexistent solvent phase in claims 9-11 in Litborn with the sample phase. This argument is partially carried over from the prior office action, where the Examiner argues that the addition of the miscible solvent in Williams to the sample phase would facilitate "mixing" of the sample phase with the immiscible cover layer phase. (Examiner's Office Action 09-29-2004, paragraph 2). In aggregate, it is unclear what exactly the Examiner is trying to state in regard to the "solvent phase"/immiscible cover liquid. Overall, the Examiner's reasoning for combining Williams and Litborn to enable this "mixing" element the Examiner reads into claims 9-11 of Litborn does not comport with the teachings in Litborn. *See, e.g.* Litborn pg 12, lines 1-3 ("Full freedom is maintained to choose the properties of the cover liquid, as long as this liquid is not miscible with the sample liquid."). On a more fundamental level, the Examiner's arguments are misdirected. The Examiner is attempting to combine Litborn and Williams based on the need to somehow enable this mixing aspect read into Litborn's claims. The teaching, suggestion or motivation to combine references must be to combine and thus produce the claimed invention, not solve some enablement problem erroneously read into the claims of the primary reference. MPEP 2143.01. The Examiner has simply never articulated why one of skill in the art would look to Williams or how one of skill would combine Williams with Litborn to solve the problem of sample volume loss in a microfluidic device. Hence, the Examiner has not carried his burden of proof for establishing a *prima facie* case of obviousness.

**II. 35 U.S.C. 103(a) as being unpatentable over Litborn and Williams et al., and further in view of Mian (6,319,469).**

Claims 9 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Litborn (WO 98/33052) and Williams et al. (5,171,989) as applied to claims 6-8, 10, 12 and 13 and further in view of Mian (6,319,469).

Litborn in combination with Williams et al. does not render obvious claims 9 or 11, for the same reasons previously discussed. As stated by the Examiner, Mian (6,319,469) discloses a microfluidic device used to analyze microsamples. However, Mian does not teach evaporation control. More specifically, Mian does not teach the use of a covering liquid to aid in preventing evaporation, or replenishing of liquid that has evaporated. Rather, Mian discloses the use of microchannels in a disk that is rotated to utilize centripetal forces to move samples in the microchannels. The invention disclosed by Mian could not even permit replenishment of liquid that has evaporated, as there is no prolonged fluid connection between the pipette barrels or hollow tubes and the inlet ports of the microfluidic device disclosed by Mian. The Examiner has failed to show, as required, that all the claimed limitations are taught or suggested by the cited references.

Furthermore, as has been previously discussed, there must be a showing of some teaching, suggestion or reason to combine the references when an obviousness determination is based on multiple prior art references. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 53 USPQ2d 1580 (Fed. Cir. 2000). In this case, there is no suggestion to combine Litborn and Williams, nor Litborn and Mian, nor a combination of the three. The Examiner has not discussed or identified any requisite suggestion to combine the references, but merely said that one would do so by reading into the references matters that are not present therein. If an Examiner continues to maintain that references contain a suggestion for their combination, the Examiner is required to make of record the passage relied upon, or state for the record that no such teaching can be found in these references. See, *In re Gartside*, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir. 2000). The Examiner's unsubstantiated and unreasoned assertion that one of skill in the art would combine these three references cannot serve to establish a *prima facie* case of obviousness. (Examiner's Office Action 09-29-2004, paragraph 3).

**CONCLUSION**

In view of the above arguments, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02149US0 from which the undersigned is authorized to draw.

Dated: October 3, 2005

Respectfully submitted,

By 

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